In the Specification:

Please replace the first paragraph of the Specification, found at page 1, lines 6 through 12, with the following amended paragraph:

This application is a divisional of U.S. Patent Application Serial No. 09/486,580, filed February 25, 2000; which is a National Stage Application based on International Patent Application No. PCT/FR98/01864, filed August 28, 1998; said PCT/FR98/01864 claims priority to French Patent Application No. FR 97/10823, filed August 29, 1997. The disclosures of each of the above-identified applications are incorporated herein by reference in their entireties, including all figures, tables, and nucleic acid/amino acid sequences.

Please replace pages 17 and 18 of the original specification with the attached substitute pages 17 and 18.

Legend to the figures

Figure 1

Genomic sequence of hDef-X (SEQ ID NO:1).

Presented is the entire genomic DNA sequence of hDef-X which exhibits significant homology with the gene encoding hDef-4 (HNP-4).

The sequence has the following sites, the presence of which is deduced by homology with the hDef-4 sequence:

| | |
|---|---|
| • CAAT box | 1711-1714 |
| • TATA box | 1758-1767 |
| • mRNA start | 1836 |
| • exon 1 | 1836-1874 |
| • splicing site 1 | GTCAGT |
| • Alu insertion | 2155-2335 |
| • L1 fragment insertion | 2710-2780 |
| • splicing site 2 | CAG |
| • exon 2 | 3394-3577 |
| • start of coding phase | 3406 |
| • splicing site 3 | GTGAGA |
| • splicing site 4 | CAG |
| • exon 3 | 4164-4379 |
| • end of coding phase | 4276 |
| • polyadenylation site | 4374-4379. |

Figure 2

Alignment of the genomic sequences of the human defensins Def-X (SEQ ID NO:1) and Def-4 (HNP-4; SEQ ID NO:7).

Alignment of the entire genomic DNA sequence of the novel defensin Def-X exhibiting homology with the genomic DNA of hDef-4 (GenBank accession number U18745).

The annotations present the positions on the hDef-4 sequence of the signals CAAT box, TATA box, splicing sites, beginning and ends of introns/exons, start of transcription and polyadenylation site.

Figure 3

Alignment of the cDNA sequences of hDef-4 (HNP-4; SEQ ID NO:8) and hDef-X (SEQ ID NO:2).

The sequences exhibit an overall homology of 61.4%. The alignment reveals an insert of about 75 bases downstream of a STOP codon, which are present on the sequence of hDef-4, but not on that of hDef-X; the strong homology continues on the whole region between the end of this insert and that of the cDNA. Outside this

insertion region, the degree of homology between nucleic sequences is therefore remarkable.

Figure 4

Peptide sequence of the protein hDef-X (SEQ ID NO:3).

The position of the sites of cleavage of the signal peptide and of the pro region were deduced from the alignment of the peptide sequences of hDef-4 and hDef-X.

Figure 5

Alignment of the peptide sequences of the known human defensins hDef-1 (SEQ ID NO:12), hDef-4 (SEQ ID NO:9), hDef-5 (SEQ ID NO:10), and hDef-6 (SEQ ID NO:11) with hDef-X (SEQ ID NO:3).

- * The star indicates an amino acid which is conserved on the five sequences.
- • The dot indicates an amino acid whose class is conserved on the five sequences (amino acid which is either identical, or which is the subject of a conservative substitution).
- ^ six arrows indicate the positions of the six cysteines conserved across the class of conventional defensins and responsible for the three-dimensional structure necessary for the activity of these peptides.

## EXAMPLES

### Example 1: Identification of the gene encoding hDef-X

Isolation of BAC B0725B12

To analyze the 8p23 region of the human genome, in particular in the region known to carry genes encoding human defensins, a BAC ("Bacterial Artificial Chromosome") corresponding to said region was isolated. A BAC library covering the complete human genome was prepared from the ADN of a human lymphoblastic line derived from individual No. 8445 of the CEPH families. This line was used as source of high-molecular weight DNA. The DNA was partially digested with the restriction enzyme BamHI, and then cloned at the BamHI site of the plasmid pBeloBacII. The clones thus obtained were "pooled" and screened according to the three-dimensional analytical procedure previously described for the screening of YAC ("Yeast Artificial Chromosome") libraries (Chumakov et al., 1992 and 1995). The three-dimensional pools obtained were screened by PCR with the aid of the primers flanking the marker SHGC-10793, for Neutrophil defensin 4 precursor (GeneBank: accession number U18745); a clone of BAC B0725 B12 was thus isolated.

After digestion with the restriction enzyme NotI, the size of the insert carried by this BAC was determined on a 0.8% agarose gel after migration by

Legend to the figures

Figure 1

Genomic sequence of hDef-X (SEQ ID NO:1).

Presented is the entire genomic DNA sequence of hDef-X which exhibits significant homology with the gene encoding hDef-4 (HNP-4).

The sequence has the following sites, the presence of which is deduced by homology with the hDef-4 sequence:

| | |
|---|---|
| • CAAT box | 1711-1714 |
| • TATA box | 1758-1767 |
| • mRNA start | 1836 |
| • exon 1 | 1836-1874 |
| • splicing site 1 | GTCAGT |
| • Alu insertion | 2155-2335 |
| • L1 fragment insertion | 2710-2780 |
| • splicing site 2 | CAG |
| • exon 2 | 3394-3577 |
| • start of coding phase | 3406 |
| • splicing site 3 | GTGAGA |
| • splicing site 4 | CAG |
| • exon 3 | 4164-4379 |
| • end of coding phase | 4276 |
| • polyadenylation site | 4374-4379. |

Figure 2

Alignment of the genomic sequences of the human defensins Def-X (SEQ ID NO:1) and Def-4 (HNP-4; SEQ ID NO:7).

Alignment of the entire genomic DNA sequence of the novel defensin Def-X exhibiting homology with the genomic DNA of hDef-4 (GenBank accession number U18745).

The annotations present the positions on the hDef-4 sequence of the signals CAAT box, TATA box, splicing sites, beginning and ends of introns/exons, start of transcription and polyadenylation site.

Figure 3

Alignment of the cDNA sequences of hDef-4 (HNP-4; SEQ ID NO:8) and hDef-X (SEQ ID NO:2).

The sequences exhibit an overall homology of 61.4%. The alignment reveals an insert of about 75 bases downstream of a STOP codon, which are present on the sequence of hDef-4, but not on that of hDef-X; the strong homology continues on the whole region between the end of this insert and that of the cDNA. Outside this

insertion region, the degree of homology between nucleic sequences is therefore remarkable.

Figure 4

Peptide sequence of the protein hDef-X (SEQ ID NO:3).

The position of the sites of cleavage of the signal peptide and of the pro region were deduced from the alignment of the peptide sequences of hDef-4 and hDef-X.

Figure 5

Alignment of the peptide sequences of the known human defensins hDef-1 (SEQ ID NO:12), hDef-4 (SEQ ID NO:9), hDef-5 (SEQ ID NO:10), and hDef-6 (SEQ ID NO:11) with hDef-X (SEQ ID NO:3).

* The star indicates an amino acid which is conserved on the five sequences.

• The dot indicates an amino acid whose class is conserved on the five sequences (amino acid which is either identical, or which is the subject of a conservative substitution).

^ six arrows indicate the positions of the six cysteines conserved across the class of conventional defensins and responsible for the three-dimensional structure necessary for the activity of these peptides.

## EXAMPLES

### Example 1: Identification of the gene encoding hDef-X

Isolation of BAC B0725B12

To analyze the 8p23 region of the human genome, in particular in the region known to carry genes encoding human defensins, a BAC ("Bacterial Artificial Chromosome") corresponding to said region was isolated. A BAC library covering the complete human genome was prepared from the ADN of a human lymphoblastic line derived from individual No. 8445 of the CEPH families. This line was used as source of high-molecular weight DNA. The DNA was partially digested with the restriction enzyme BamHI, and then cloned at the BamHI site of the plasmid pBeloBacII. The clones thus obtained were "pooled" and screened according to the three-dimensional analytical procedure previously described for the screening of YAC ("Yeast Artificial Chromosome") libraries (Chumakov et al., 1992 and 1995). The three-dimensional pools obtained were screened by PCR with the aid of the primers flanking the marker SHGC-10793, for Neutrophil defensin 4 precursor (GeneBank: accession number U18745); a clone of BAC B0725 B12 was thus isolated.

After digestion with the restriction enzyme NotI, the size of the insert carried by this BAC was determined on a 0.8% agarose gel after migration by